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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,740	12/24/2003	Eiichi Iishi	1422-0619P	9686

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EXAMINER	
HABTE, KAHSAY	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 05/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/743,740	IISHI ET AL.	
	Examiner	Art Unit	
	Kahsay Habte, Ph. D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/23/04 & 3/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-3 are pending.

Response to Amendment

2. Applicant's amendment filed 3/22/2005 in response to the previous Office Action (9/24/2004) is acknowledged. Rejections of claims 1-2 under 35 U.S.C. 102(b) has been maintained.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaspersen *et al.* {Journal of Label. comp. and Radiopharm., 27, No. 9, 1055 (1989)}. Kaspersen et *al.* teaches the multi-step synthesis of Org-3770 (mirtazapine) on page 1058 (Fig.4). On page 1066, Kaspersen *et al.* also teaches the crystallization of the mirtazapine from the crude product using methanol/water solvent mixture to achieve almost pure crystals. Claims 1-3 are product claims, in which applicants recite some of the physical and chemical characteristics of the said product. MPEP 2112 says:

"SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE UPON THE DISCOVERY OF A NEW PROPERTY

The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)."

In this case, the "unknown property" is the particular crystalline form with X-ray diffraction pattern and the level of dryness. This is unknown because the reference is silent on this property. MPEP 2112 goes on to state:

"A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection."

Again, the "CHARACTERISTIC" which the prior art is silent on is the crystalline form.

This is not an ordinary inherency situation where it is not explicitly stated what the product actually is. Here the reference explicitly teaches exactly what the compound is. The only difference is a characteristic about which the reference happens to be silent. See also Ex parte Anderson, 21 USPQ 2nd 1241 at 1251.

Applicants are reminded that the PTO has no testing facilities. If applicants' reasoning were accepted, then any anticipation rejection of an old compound could always be overcome by tacking on some characteristic or property which the reference was silent on, regardless of whether the prior art material was any different from the claimed material. For example, if it did not happen to mention the color, one could patent an old compound just by adding "which is green" or "which is not indigo". One could put in a limitation about density (e.g. "density is not 1.4"), melting point, "refractive index of 2.0", solubility in some obscure solvent, spectroscopic data, and then simply point to the silence of the reference, as applicants have done here. Or one could add properties like or "does not explode on tapping" or "in the form of microneedles" or, as here, "crystals have characteristic diffraction peaks in the X-ray diffraction pattern."

Response to arguments

Applicant's argument filed 3/22/2005 has been fully considered but it is not persuasive.

Applicants argue "[t]he Examiner must provide factual and technical grounds establishing that the inherent features ***necessarily*** flows from the teachings of the prior art.....holding that inherency ***must flow as a necessary conclusion from the prior art, not simply a possible one.***" The examiner disagrees with this argument. The anticipation is based on inherency see MPEP 2112. The inherency is not based on a possible conclusion, but based on facts. Applicants are claiming low–hygroscopic anhydrous mirtazapine crystals that are presumed to be the same as the crystals

obtained by Kaspersen. Since applicants did not show that their compounds are different from the prior art compound, it is assumed that the prior art compound is the same as applicants.

Applicants argue: "[b]ased upon the following comments and observations, that the presently claimed anhydrous crystals are not necessary conclusion from the teaching of Kaspersen. Specifically, the drying conditions of Kaspersen would not necessarily provide mirtazapine crystals having (i) water content of not more than 0.5 % by weight and (ii) a hygroscopic degree of not more than 0.6% by weight when the crystals are stored in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours, as presently claimed". Applicants refer to Kaspersen's drying conditions and conclude: "Kaspersen dries the mirtazapine composition under conventionally used conditions which are designed to be gentle to avoid decomposition which is thought to occur at high temperature. Therefore, the mirtazapine hydrate has been dried under ordinary drying conditions.....However, when the mirtazapine is dried at such low temperature, anhydrous mirtazapine crystals satisfying both (i) water content of not more than 0.5 % by weight and (ii) a hygroscopic degree of not more than 0.6% by weight cannot be obtained". The examiner disagrees with this conclusion, since the argument is not relevant to the issue. Applicants are claiming a compound (i.e. anhydrous mirtazapine crystals), but not a method of making the low-hygroscopic anhydrous mirtazapine crystals. Thus, any argument that has to do with how the mirtazapine is dried or stored is irrelevant to the issue. Applicants are not claiming a method.

Applicants argue that they have found through tireless efforts and supreme ingenuity anhydrous mirtazapine crystals having (i) and (ii), because the mirtazapine hydrate is dried under "special" drying conditions (e.g. high temp. 90°C to 95°C and under low pressure of 1330 to 1862 Pa as disclosed in Example 7 of the specification). Applicants also refer to Example 8, in which drying at ordinary temperature (50°C - 60°C) and reduced pressure (4 - 5.3 kpa) resulted crystals of a hydrate having a relatively higher water content of 3.5% and failed to give anhydrous mirtazapine crystals having (i) and (ii). The examiner disagrees with this conclusion for the reasons discussed above. Applicants indicate that Example 8 of the specification resulted crystals (not more than 3.5% by weight) that are dried under reduced pressure and ordinary temperature, but it is unclear how this relevant in overcoming Kaspersen.

Note that because applicant's "special" drying conditions resulted in low-hygroscopic low-hygroscopic anhydrous mirtazapine crystals having (i) water content of not more than 0.5 % by weight and (ii) a hygroscopic degree of not more than 0.6% by weight when the crystals are stored in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours, does not mean applicant's compound is different from the prior art compound. Applicant's compound would be different from the prior art compound (Kaspersen) if the "special" drying conditions when applied to the prior art compound gave a different property from what is claimed.

Applicants reasoning appears to be that only his technique (e.g. special drying condition) can produce a mirtazapine crystal with (i) water content of not more than 0.5 % by weight and (ii) a hygroscopic degree of not more than 0.6% by weight when the

crystals are stored in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours. This is unpersuasive. Even though Kaspersen mirtazapine is not exposed to applicants' specific techniques, it does not mean other techniques cannot give anhydrous mirtazapine with same property (i.e. (i) and (ii)). There is no evidence that only applicants' techniques will produce this property.

Applicants also argue that that compound 1c is "labeled" compound and the mirtazapine of the present invention is an "unlabeled" compound. The examiner disagrees with applicants. Carbon 13 has the natural abundance of 1%; that is, approximately 1% of all the carbon atoms in any sample of an organic compound are carbon-13 atoms. The intended purpose for both the labeled and unlabeled mirtazapines is not significantly different one from the other. Note that the labeled compound was prepared in order to study what the known unlabelled compound does in the body and, thus, use of unlabeled compounds would also be obvious as this is normal form. See previous Office Actions in the parent case (09/697,329) more detail.

Since applicants have not presented any evidence that their compound is different from Kaspersen's, the rejection has been maintained. Applicants have to replicate Kaspersen and apply "special drying conditions" on the resulting crude mirtazapine, in order to conclude that Kaspersen's does not posses (i) water content of not more than 0.5 % by weight and (ii) a hygroscopic degree of not more than 0.6% by weight".

Applicant's compound has passed the test (i.e. the hygroscopic degree was not more than 0.6% by weight when the crystals are stored in the air having a relative

humidity of 75% at 25°C under atmospheric pressure for 500 hours), but this test was not done on the prior art compound. In order to overcome this rejection, applicants have to do the test that comprise storing Kaspersen's mirtazapine crystals in the air having a relative humidity of 75% at 25°C under atmospheric pressure for 500 hours and conclude that the hygroscopic degree after the test is no more than 0.6% by weight. If the hygroscopic degree is less than 0.6% after the test, the rejection will be maintained.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte, Ph. D. whose telephone number is (571) 272-0667. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on (571) 272-0674, if there is no reply within 24 hours, James Wilson (Acting SPE) can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kahsay Habte, Ph. D.
Examiner
Art Unit 1624

Mark L. Berch
Primary Examiner
Art Unit 1624

KH
May 4, 2005